

CLAIMS

What is claimed is:

1. A method of identifying a molecule involved in lipid regulation comprising identifying a molecule that binds to, or that inhibits binding of a molecule to, HBM or Zmax1.
2. ~~The method of claim 2, wherein said molecule is a protein.~~
3. The method of claim 2, further comprising producing an antibody to the protein.
4. A method for identifying a protein involved in lipid regulation comprising identifying a protein that has an expression level that is different in a first host comprising the *Zmax1* gene when compared to a second host comprising the *HBM* gene.
5. The method of claim 4, wherein the host is an animal.
6. A method for identification of a candidate molecule involved in lipid regulation comprising:
 - (A) identifying a molecule that binds to, or that inhibits binding of a molecule to, the nucleic acid sequence of SEQ ID NO: 1 or a Zmax1 nucleic acid comprising a polymorphism of Table 4;
 - (B) identifying a molecule that binds to, or that inhibits binding of a molecule to, the nucleic acid sequence of SEQ ID NO: 2; and
 - (C) comparing the extent of binding, or the extent of inhibition of binding, of the molecule to each nucleic acid sequence, wherein the molecule that binds, or inhibits binding, more or less to the nucleic acid sequence of SEQ ID NO: 2 or the nucleic acid sequence of

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SEQ ID NO: 1 or a Zmax1 nucleic acid comprising a polymorphism of Table 4 is the candidate molecule.

7. The method of claim 6, wherein the candidate molecule is a protein, an mRNA or an antisense nucleic acid.

8. A method for testing a substance as a therapeutic agent for modulating lipid levels comprising administering a nucleic acid comprising SEQ ID NO: 2 or a nucleic acid sequence with an HBM polymorphism to a subject, and assessing whether lipid levels are modulated.

9. The method of claim 8, wherein the subject is an animal and the animal is selected from the group consisting of: livestock, primates, humans, canines, felines, rodents, birds, reptiles, fish, and amphibians.

10. A method for testing a substance as a therapeutic agent for modulating lipid levels comprising administering a protein comprising SEQ ID NO: 4 or a Zmax1 protein comprising a polymorphism of Table 4 to a subject, and assessing whether lipid levels are modulated.

11. A method of pharmaceutical development for treating lipid-mediated disorders comprising identifying a molecule that binds to the amino acid sequence of SEQ ID NO: 4 or to a Zmax1 protein comprising a polymorphism of Table 4.

12. The method of claim 11, wherein the molecule inhibits or enhances the function of the amino acid.

13. A method of pharmaceutical development for treatment of lipid-mediated disorders comprising:

- (A) constructing a first host that contains the *Zmax1* gene or protein;
- (B) constructing a second host that contains the *HBM* gene or protein;
- (C) analyzing a difference between the first host and the second host; and
- (D) identifying a molecule that, when added to the first host, causes the first host to exhibit a characteristic feature of the second host.

14. The method of claim 13, wherein the host is a cell-free extract, a cell or an animal.

15. The method of claim 13, wherein the difference is a surrogate marker.

16. A method of regulating lipid levels in a host comprising administering the amino acid sequence comprising SEQ ID NO: 4 to a somatic cell or to a germ-line cell of a host suffering from a lipid-mediated disorder.

17. The method of claim 16, wherein the host is livestock, primates, humans, canines, felines, rodents, birds, reptiles, fish, or amphibians.

^{18.}
~~19.~~ A method for treating or preventing a lipid-mediated disorder in an animal comprising transferring a nucleic acid sequence comprising SEQ ID NO: 2 or a *Zmax1* nucleic acid comprising a polymorphism of Table 4 into a somatic cell or a germ-line cell of an animal suffering from a lipid-mediated disorder.

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19.
~~20.~~ The method of claim ~~19~~¹⁸, wherein the animal is livestock, primates, humans, canines, felines, rodents, birds, reptiles, fish, or amphibians.

^{20.}
~~21.~~ A method of treating or preventing arteriosclerosis or an arteriosclerosis-associated condition comprising administering an amino acid sequence comprising SEQ ID NO: 4 to a patient in need thereof.

²¹/₂₂. The method of claim ²⁰/₂₁, wherein the patient is livestock, primates, humans, canines, felines, rodents, birds, reptiles, fish, or amphibians.

²²/₂₃. The method of claim ²⁰/₂₁, wherein the amino acid sequence administered to a patient in need thereof comprises the extracellular domain of the amino acid sequence comprising SEQ ID NO: 4.

²³/₂₄. The method of claim ²⁰/₂₁, wherein the amino acid sequence administered to a patient in need thereof comprises the intracellular domain of the amino acid sequence comprising SEQ ID NO: 4.

²⁴/₂₅. A method for treating or preventing a lipid-mediated disorders comprising administering a molecule that binds to a nucleic acid sequence comprising SEQ ID NO: 2 or a Zmax1 nucleic acid comprising a polymorphism of Table 4 to a patient in need thereof.

²⁵/₂₆. The method of claim ²⁴/₂₅, wherein the patient is livestock, primates, humans, canines, felines, rodents, birds, reptiles, fish, or amphibians.

²⁶/₂₇. A method for treating or preventing lipid-mediated disorders comprising administering an antibody to a patient in need thereof, wherein the antibody is to the amino acid sequence comprising SEQ ID NO: 4.

²⁷/₂₈. A method for diagnostic screening for a genetic predisposition to arteriosclerosis or an arteriosclerosis associated condition or a lipid-mediated disorder comprising screening a sample from a patient with a nucleotide sequence derived from the genomic or cDNA nucleic acid sequence of HBM.

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~~28.~~ The method of claim ²⁷~~28~~, wherein the screening involves performing a haplotype analysis using the nucleic acid sequence comprising SEQ ID NO: 2 and determining whether the subject contains the *Zmax1* gene or lacks an HBM polymorphism.

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~~30.~~ A diagnostic assay for determining a predisposition for a lipid-mediated disorders comprising an antibody to the HBM protein and an antibody to the *Zmax1* protein.

³⁰
~~31.~~ A method of expressing the HBM protein in tissue comprising constructing an expression vector comprising a promoter that directs expression in tissue operably linked to SEQ ID NO:2 and the tissue in which the HBM protein is expressed is a lipid regulating cell or a cell involved in lipid metabolism.

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~~32.~~ The method of claim ³⁰~~31~~, wherein the tissue is liver.

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~~33.~~ The method of claim ³⁰~~31~~, wherein the promoter that directs expression in tissue is an osteocalcin promoter or an AML-3 promoter.

³³
~~34.~~ A method of modulating lipid levels in a subject by administering an HBM protein or a *Zmax1* protein comprising a polymorphism of Table 4.

³⁴
~~35.~~ The method of claim ³³~~34~~, wherein the HBM protein comprises SEQ ID NO: 4.

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~~36.~~ The method of claim ³³~~34~~, wherein the lipid modulated is selected from the group consisting of: VLDL, LDL, IDL, HDL, LIPOa, APO A-1, APO B and APO E.

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~~37.~~ A method of modulating lipid levels in a subject by administering an agent which regulates HBM or *Zmax1* activity.

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37.
38. The method of claim 37, wherein the lipid modulated is selected from the group consisting of: VLDL, LDL, IDL, HDL, LIPOa, APO A-1, APO B and APO E.

38.
39. The method of claim 37, wherein the regulation of HBM or Zmax1 activity is modulates gene transcription, protein translation or Zmax1 or HBM protein binding to its cognate target thereby regulating lipid levels.

39.
40. A composition for treating a lipid-mediated condition comprising an agent that modulates lipid levels by regulating Zmax1 or HBM activity and a lipoprotein modulating agent with a pharmaceutically acceptable carrier.

40.
41. The composition of claim 40, wherein the lipoprotein modulating agent is blofibrate, gemfibrozil, nicotinic acid, cholestyramine, cholestipol, lovastatin, simvastatin, pravastatin, probucol, premarin or estradiol.

41.
42. The composition of claim 40, wherein the lipoprotein modulating agent modulates LDL levels.

42.
43. The composition of claim 42, wherein the lipoprotein modulating agent is selected from the group consisting of bile acid binding resins, HMG-CoA reductase inhibitors and estrogens.

43.
44. A method of treating a subject suffering from a lipid-mediated condition comprising the step of administering the composition of claim 40.

44.
45. The method of claim 44, wherein the lipid-mediated condition is atherosclerosis, arteriosclerosis, or a disease associated with atherosclerosis or arteriosclerosis.

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~~46~~. A combination therapy for treating a subject suffering from a lipid-mediated disease or condition comprising administering to a subject an agent which regulates HBM or Zmax1 and an agent which regulates a lipoprotein.

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~~47~~. The combination therapy of claim ⁴⁵~~46~~, wherein the agent regulating lipoprotein concentrations is blofibrate, gemfibrozil, nicotinic acid, cholestyramine, cholestipol, lovastatin, simvastatin, pravastain, probucol, premarin or estradiol.

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~~48~~. The method of claim ⁴⁵~~46~~, wherein the lipid-mediated disease is atherosclerosis, arteriosclerosis, an atherosclerosis associated condition or an arteriosclerosis associated condition.